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Letter to the Editor: Nutritional Status of Children With Leukemia

We read with interest the paper of Yu et al. [1], "Nutritional Status of Children With Leukemia," which appeared in *Medical and Pediatric Oncology*, and contribute this article with our local experience in a similar patient group.

Pediatric cancer patients represent a high-risk group for protein energy malnutrition [2]. Mild or marginal malnutrition must be identified to prevent the development of severe protein-energy malnutrition in pediatric cancer patients. We evaluated the nutritional status and determined that the daily energy, protein, and micronutritient intake identified mild or marginal malnutrition in 45 pediatric cancer patients (25 in remission, 20 newly diagnosed or relapsed). Ninety-five percent of patients consumed energy and 35.5% of them consumed protein less than the recommended dietary allowance (RDA). We showed that 36.7–84.6% of patients consumed various vitamins and 75.8–89.1% consumed minerals less than the RDA.

Nutritional status was evaluated with anthropometric measurements and biochemical indices [1,3]. According to the weight-for-height index, 23 of 45 children (51.1%) were determined as malnutriated: 23 (28.9%) showed advanced malnutrition, 5 (11.1%) moderate malnutrition, and 4 (11.1%) mild malnutrition. In developed countries it has been estimated that malnutrition is seen in 8–32% of pediatric cancer patients. In Turkey there are various problems associated with educational status, traditional nutritional habits of families, and environmental conditions. Therefore, malnutrition continues to be a major problem in Turkey, although its frequency decreases [4]. In chronic diseases like cancer, risk of malnutrition is very high. With this study, in 51.1% of pediatric cancer patients, malnutrition according to the weight-for-height index was determined with a higher ratio than your study group.

Although in our study group malnutrition is commonly determined by weight-to-height ratios, serum albumin levels of all children were found to be normal (Table I). However, serum albumin levels were lower in the active disease group than in the remission group ($P < 0.05$). These results suggested that albumin was not a reliable indicator in the early diagnosis of malnutrition in pediatric cancer patients, but may reflect acute metabolic response to active disease.

Transferrin levels were less than 200 mg/dl in 17.8% of patients. Serum transferrin levels were not significantly different in the two groups (Table I). These results suggested that transferrin was not a reliable indicator in the early diagnosis of malnutrition in pediatric cancer patients.

Yu et al. [1] reported that prealbumin is the most sensitive indicator of visceral protein status in leukemic patients. We found that absolute prealbumin levels were 19.4 ± 7.2 mg/dl in the remission group and 14.8 ± 5.1 mg/dl in the active disease group (Table I) ($P < 0.05$). The mean relative prealbumin values (observed value/expected value $\times$ 100) were 74.3 ± 29.1 in the remission group and 58.1 ± 23.3 in the active disease group ($P < 0.05$). Children in the active disease group had lower prealbumin values compared to children in the remission group, suggesting that the activity of disease may affect the nutritional state of the children with malignancy. In our study group, 80.0% of patients with mild malnutrition had low relative prealbumin values, verifying that prealbumin is a reliable and sensitive indicator of mild and marginal malnutriton. According to anthropometric measurements, 69.6% of patients with normal nutritional status had low prealbumin values. This finding suggests that low prealbumin may be found before prealbumin values. This finding suggests that low prealbumin may be found before malnutrition is detected by anthropometric measurements and low prealbumin values may indicate the necessary planning of nutritional intervention.

Nutritional support provided after malnutrition occurs is intolerable because of insufficient intake and it is usually hard to cover up the deficiency. Therefore, it is important to prevent malnutrition before it occurs. We observed that patients in normal nutritional status consumed only 52.7% of recommended energy. This observation suggests that nutritional deficiency had occurred in our patients before malnutrition was detected by anthropometric measures.

We conclude that malnutrition is common in pediatric cancer patients and prealbumin is a reliable and sensitive indicator of mild and marginal malnutrition. Determining prealbumin values and assessing the deficiency of micro- and macronutrients before malnutrition is detected by anthropometric measures suggest that nutritional problems may occur and it is necessary to plan nutritional intervention in pediatric cancer patients.

Zafer Kurugol, MD
Ayten Egemen, MD
Department of Social Pediatrics
Nazan Çetingul, MD
Senay Oztop, MD
Department of Pediatric Oncology

TABLE I. Biochemical Measurements in Pediatric Cancer Patients†

Biochemical measurements	Remission group (n = 25)	Active disease group (n = 20)	Total (n = 45)
Creatinine (mg/dl)	0.6 ± 0.2	0.5 ± 0.1	0.5 ± 0.1
Albumin (g/dl)	4.7 ± 0.6	4.3 ± 0.6*	4.5 ± 0.6
Transferrin (mg/dl)	253 ± 87	255 ± 68	254 ± 78
Prealbumin (mg/dl)	19.4 ± 7.2*	14.8 ± 5.1*	16.8 ± 5.3
Relative prealbumin (%)	74.3 ± 29.1*	58.1 ± 23.3*	63.0 ± 19.9

†Relative prealbumin = observed prealbumin/expected prealbumin × 100; expected prealbumin values for age and sex are those of Bevenga et al. [5].
*$P < 0.05$; the means of the active disease group were significantly different from those of the remission group for prealbumin and relative prealbumin by Student's t-test.

Kaan Kavakli, MD
Gungor Nişli, MD
Department of Pediatric Hematology
Ege University Medical School
35100 Bornova, Izmir, Turkey

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Letter to the Editor: Cryopreservation of Semen From Adolescent Patients With Malignancies

The article by Kliesch [1] et al. prompts us to draw the attention of your readers to the results of our investigations which were published in Medical and Pediatric Oncology in 1988 [2]. Unfortunately, reference to our study was not made in Table 2 of the Kliesch publication which summarized reports on semen parameters and pregnancy outcome in male patients with malignancies during childhood or adolescence since 1980.

Our communication involved 27 male long-term survivors of childhood cancer treated during the prepubertal or pubertal period. Among these, information was provided on the semen analysis of 23. Four patients refused to provide specimens, but indicated that they had fathered normal healthy children. The study appeared to be the first investigation in which an attempt was made to analyze the effects of single or multi-agent chemotherapy in terms of cumulative doses per surface area and sperm production for reproductive function. Hormonal levels were also analyzed. The results revealed that aspermia could be induced by large (cumulative) doses of single alkylating agents, small (cumulative) doses of multiple alkylating agents, and additive antispermatogonial activity of (other) alkylating and nonalkylating agents. Notwithstanding, despite the administration of established or putative sterilizing agents, sterility was not absolute or definite. Thus, normal reproduction function was observed in at least two patients who received an approximate cumulative dose of 30 g/m^2 of cyclophosphamide. The latter differed from our earlier assessments in which 20 mg/m^2 of cyclophosphamide could induce sterilization. As a consequence, we suggested that other undefined factors also had to be considered and that the certitude of sterility or potency could not be predicted. We were also unable to correlate or predict male fertility by clinical examination (testicular size), gonadatrophin, or testosterone values.

Additional follow-up of the above experience has revealed that patients 4, 12, and 15 in the communication are probably sterile, since they still have not fathered children. Their reproductive capacities were considered questionable at the time of publication. However, patient 13, who was considered questionably sterile, has fathered a child (sperm concentration 5.6 million per ml at the time of publication).

Recent communications have also demonstrated that dose intensity is an important determinant of response to treatment [3,4]. The former is a function of dose, schedule and treatment duration. Indeed, it may also be a major determinant of potential side effects [5]. The possibility of

investigating this parameter as an additional component of treatment, induced sterility should also be considered.

The above experiences and the additional follow-up again emphasize the conclusions of our communication: fertility potential cannot be predicted with certainty by clinical examination (testicular size), gonadatrophin, and testosterone values. While alkylating agents and radiation therapy may indeed cause sterility, their effects may not be absolute. These factors also indicate that additional investigations are urgently required to establish more accurate correlation of dosage and male reproductive potential.

Hubert L. Ried, MD
Hallie Zietz, RN, PNP
Norman Jaffe, MD, DSc

University of Texas, M.D. Anderson Cancer Center
Department of Pediatrics, Box 87
1515 Holcombe Boulevard,
Houston, TX 77030

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